```
OM of: US-09-525-998A-1 to A_Geneseq_1101.*   out_format : pfs

Date: Apr 23, 2002 10:13 PM

About: Results were produced by the GenCore software, version 4.5,
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Command line parameters:
 -MODEL-frame+_n2p.model -DEV-xlp
 -Q=[illegible]_1/USPTO_spool/[illegible]_23042002_1[illegible]37_18179/app_query.fasta_1.[illegible]
 -DB-A_Geneseq_1101 -QFMT-fastan -SUFFIX=rag -GAPOP=12.000
 -GAPEXT-4.000 -MINMATCH-0.100 -LOOPCL=0.000 -LOOPEXT-0.000
 -QGAPOP-4.500 -QGAPEXT-0.050 -XGAPOP=10.000 -XGAPEXT=0.500
 -FGAPOP-6.000 -FGAPEXT-7.000 -YGAPOP=10.000 -YGAPEXT=0.500
 -DELOP=6.000 -DELEXT-7.000 -START=1 -MATRIX-blosum62
 -TRANS-human40.cdi -LIST=45 -DOCALIGN=200 -THR_SCORE-pct
 -THR_MAX-100 -THR_MIN=0 -ALIGN=15 -MODE=LOCAL -OUTFMT=pfs
 -NORM-ext -MINLEN-0 -MAXLEN=2000000000
 -USER-US09525998_@CGN1_1_77  NCPU-6 -ICPU-3  LONGLOG -NO_XLPXY
 -WAIT -THREADS=1

Search information block:
Query: US-09-525-998A-1
Query length: 1368
Database: A_Geneseq_1101:*
Database sequences: 522463
Database length: 74073290
Search time (sec): 140.140000


score_list:
Sequence                 Strd Orig     ZScore   EScore Len  ! Documentation
/SIDS2/gcgdata/geneseq/geneseqp/AA1991.DAT:AAR10986 + 2487.00 3659.12  1.7e-196  455  !
/SIDS2/gcgdata/geneseq/geneseqp/AA1993.DAT:AAR4[illegible] + 2487.00 3659.12  1.7e-196  455  !
/SIDS2/gcgdata/geneseq/geneseqp/AA1995.DAT:AAR75084 + 2487.00 3659.12  1.7e-196  455  !
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seq_documentation_block:
ID   AAR10986 standard; Protein; 455 AA.
XX
AC   AAR10986;
XX
DT   13-MAY-1991  (first entry)
XX
DE   30kD TNF inhibitor precursor.
XX
KW   Tumour necrosis factor, inhibitor.
XX
OS   Homo sapiens.
XX
FH   Key                Location/Qualifiers
FT   Cleavage-site      40..41
FT                      note=" cleavage gives active protein "
XX
PN   AU9058976-A.
XX
PD   24-JAN-1991.
XX
PF   16-JUL-1990;    90AU-0058976.
XX
PR   07-FEB-1990;    90US-0479661.
PR   18-JUL-1989;    89US-0381080.
PR   12-DEC-1989;    89US-0450229.
XX
PA   (SYNE-) SYNERGEN INC.
XX
DR   WPI; 1991-057847/11.
DR   N-PSDB; AAQ10883.
XX
PT   Tumour necrosis factor inhibitor - for suppression of TNF-alpha
PT   and beta, useful as therapeutic agent.
XX
PS   Disclosure; Fig 21; 142pp; English.
XX
CC   The sequence comprises the entire 30 kD TNF inhibitor. The clone
CC   from which the sequence was deduced was isolated from a cDNA
CC   library prepd. from RNA form U937 cells treated with PMA/PHA.
CC   The whole gene can be inserted into expression vectors for prepn.
CC   of TNF inhibitor for use in the treatment of inflammatory and
CC   degenerative diseases. The active protein is claimed (Claim 8).
CC   See also AAR10984 and AAR11001.
XX
SQ   Sequence   455 AA;


alignment_scores:
           Quality: 2487.00             Length:     455
             Ratio:    5.466              Gaps:       0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-1 x AAR10986 ..

 Align seg 1/1 to: AAR10986 from: 1 to: 455

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       1 MetGlyLeu[illegible]rThrValProAspLeuLeuLeuProLeuValLeuLeuGl 17

      51 [illegible]ACC 100
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      17 [illegible] 34
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  34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

 151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
     ||||||||||||||||||||||||||||||||||||||||||||||||||
  51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

 201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
     ||||||||||||||||||||||||||||||||||||||||||||||||||
  67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

 251 GTCAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
     ||||||||||||||||||||||||||||||||||||||||||||||||||
  84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

 301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

 351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

 401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

 451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

 501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

 551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
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 601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
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 201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

 651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234

 701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250

 751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
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 251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

 801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
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 267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

 851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
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 284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300

 901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
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 301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317

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 317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334

1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

1051 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367

1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384

1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
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 401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417

1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450

1351 CCCAGTCTTCTCAGA 1365
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 451 ProSerLeuLeuArg 455

seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA1993.DAT:AAR42059

seq_documentation_block:
ID   AAR42059 standard; Protein; 455 AA.
XX
AC   AAR42059;
XX
DT   29-APR-1994  (first entry)
XX
DE   Lambda derived TNF-R.
XX
KW   Human; tumour necrosis factor receptor; TNF-R; interleukin-1 receptor;
KW   IL-1R; fusion protein; linker; TNF; IL-1; cachexia; cerebral malaria;
KW   rheumatoid arthritis; diabetes; multiple sclerosis, septic shock;
KW   pulmonary fibrosis; silicosis; allograft; xenograft; rejection;
KW   graft verses host disease; sepsis; inflammation; allergy;
KW   autoimmune dysfunction.
XX
OS   Homo sapiens.
OS   Lambda-gt10-7ctufbp.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..40
FT                   /note= "Signal peptide"
FT   Protein         41..455
FT                   /note= "Mature hTNF-R"
XX
PN   WO9319777-A.
XX
PD   14-OCT-1993.
XX
PF   26-MAR-1993;   93WO-US02938.
XX
PR   30-MAR-1992;   92US-0860710.
XX
PA   (IMMV ) IMMUNEX CORP.
XX
PI   Smith CA;
XX
DR   WPI; 1993-336592/42.
DR   N-PSDB; AAQ49932.
```

```
XX
PT   New fusion protein tumour necrosis factor and human interleukin-1
PT   receptor - useful in therapy, diagnosis and assays of e.g.
PT   rheumatoid arthritis, diabetes, cerebral malaria, sepsis, etc.
XX
PS   Disclosure; Page 57-59; 85pp; English.
XX
CC   The sequences given in AAR42058-59 repressent human tumour necrosis
CC   factor receptor (TNF-R) and the sequences in AAR42060-61 represent
CC   human interleukin-1 receptor (IL-1R).  These sequences were used in
CC   the production of a fusion protein which conformed to one of the
CC   formulae:
CC        TNF-R-linker-TNF-R-linker-IL 1R
CC        IL-1R-linker-TNF-R-linker-TNF-R or
CC        TNF-R-linker-TNF-R
CC   The linker may comprise 5-100 amino acids selected from Gly, Asp,
CC   Ser, Thr and Ala.  These linkers separate the individual moeities
CC   by such a distance that each component of the fusion protien is
CC   capable of folding into the secondary or tertiary structure required
CC   for its biological activity.  These fusion proteins may be used in
CC   therapy, diagnosis and assays for conditions mediated by TNF or IL-1,
CC   particularly in conditions in which both TNF and IL-1 play a causitive
CC   role.  They may be used to treat cachexia, rheumatoid arthritis,
CC   diabetes, multiple sclerosis, pulmonary fibrosis and silicosis,
CC   cerebral malaria, allograft and xenograft rejection in graft verses
CC   host disease, sepsis, septic shock, inflammation, allergies and
CC   autoimmune dysfunctions.
XX
SQ   Sequence   455 AA;


alignment_scores:
          Quality: 2487.00           Length:    455
            Ratio:   5.466             Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-1 x AAR42059   ..

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        ||||||||||||||||||||||||||||||||||||||||||||||||||
     17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

    101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGTCCCCAAGGAAAATATATC 150
        ||||||||||||||||||||||||||||||||||||||||||||||||||
     34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

    151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
        ||||||||||||||||||||||||||||||||||||||||||||||||||
     51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

    201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
        ||||||||||||||||||||||||||||||||||||||||||||||||||
     67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

    251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
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     84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

    301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

    351 CACACTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
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    117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

    401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTTAATTGCAGCCTCTGCCTC 450
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

    451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

    501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

    551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

    601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

    651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234

    701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250

    751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

    801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

    851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300

    901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317

    951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334

   1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

   1051 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367

   1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384

   1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

   1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417

   1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

   1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
```

```
           ||||||||||||||||||||||||||||||||||||||||||||||||||
       434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450

      1351 CCCAGTCTTCTCAGA 1365
           |||||||||||||||
       451 ProSerLeuLeuArg 455

seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA1995.DAT:AAR75084

seq_documentation_block.
ID   AAR75084 standard; Protein; 455 AA.
XX
AC   AAR75084;
XX
DT   19-JAN-1996  (first entry)
XX
DE   p55 TNF-R.
XX
KW   p55; tumour necrosis factor receptor; TNF-R; human; murine; chimera,
KW   epidermal growth factor receptor; EGF-R; protease; inhibitor;
KW   phorbol myristate acetate; PMA.
XX
OS   Homo sapiens.
XX
FH   Key              Location/Qualifiers
FT   Peptide          41..53
FT                    /note= "N terminus of soluble p55 TNF-R"
FT   Modified-site    54..56
FT                    /note  "glycosylation site"
FT   Modified-site    145..147
FT                    /note= "glycosylation site"
FT   Modified-site    161..163
FT                    /note= "glycosylation site"
FT   Peptide          193..210
FT                    /note= "peptide used in creation of chimeras"
FT   Region           198..210
FT                    /note  "spacer region"
FT   Misc-difference  201
FT                    /note= "major C terminus for soluble p55 TNF-R"
FT   Misc-difference  202
FT                    /note= "essential for shedding reaction'
FT   Misc-difference  203
FT                    /note= "minor C terminus for soluble p55 TNF-R"
FT   Region           212..234
FT                    /note= "transmembrane region"
XX
PN   AU9475742-A.
XX
PD   04-MAY-1995.
XX
PF   11-OCT-1994;   94AU-0075742.
XX
PR   12-OCT-1993;   93IL-0107268.
XX
PA   (YEDA ) YEDA RES & DEV CO LTD.
XX
PI   Batkin M,  Brakebusch C,  Varfolomeev E,  Wallach D;
XX
DR   WPI; 1995-194342/26.
DR   N PSDB, AAQ90513.
XX
PT   New protease capable of cleaving soluble tumour necrosis factor
PT   (TNF) receptor  - from cell-bound TNF- receptor, useful for
PT   antagonising deleterious effects of TNF.
XX
PS   Disclosure; Fig 1; 40pp; English.
XX
CC   This sequence represents human p55 tumour necrosis factor (TNF-R).
CC   Expression of this receptor is regulated by shedding of the
CC   extracellular receptor fragment.  The p55 TNF-R can be shed in response
CC   to different inducing agents, e.g. phorbol myristate acetate (PMA),
CC   depending on cell type.  The only region of the receptor whose structure
CC   affects the shedding response is the spacer region (see AAR75012) in the
```

```
CC   extracellular domain.  This region is located close to a site of cleavage
CC   of the molecule, and links the Cys rich module to the transmembrane
CC   domain.  The spacer region of the encoded protein was used to create the
CC   chimeras between human p55 TNF-R and murine epidermal growth factor
CC   receptor (EGF-R) that are represented by AAR75007-11.  This spacer region
CC   was subjected to deletion mutations (AAR75013-25) and substitutions
CC   (AAR75026 47).  Of the spacer region, the most important residues are
CC   Asn 172, Val 173, Lys 174 and Gly 175  with Val 173 being the most
CC   important of these.  The shedding of the receptor is independent of the
CC   side chain identity of these residues, with the exception of a limited
CC   dependence on the identity of Val 173.  Mutations which alter the
CC   conformation of the protein adversely effect the shedding process.
CC   The mutations shown in AAR75013-47 were introduced in order to create an
CC   inhibitor of a protease that is capable of cleaving the soluble TNF-R
CC   from the cell bound TNF-R.  Fragments of these inhibitors can be seen in
CC   AAR75017-9, AAR75025, AAR75033-5 and AAR75042-3.  These protease
CC   inhibitors can be used for enhancing TNF function.
XX
SQ   Sequence   455 AA;


alignment_scores:
             Quality: 2487.00            Length:    455
               Ratio:  5.466               Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
  US-09-525-998A-1 x AAR75084    ..

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        51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGACTGGTCCCTCACC 100
           ||||||||||||||||||||||||||||||||||||||||||||||||||
        17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

       101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGTCCCCAAGGAAAATATATC 150
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       151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
           ||||||||||||||||||||||||||||||||||||||||||||||||||
        51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

       201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
           ||||||||||||||||||||||||||||||||||||||||||||||||||
        67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

       251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||
        84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

       301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
           ||||||||||||||||||||||||||||||||||||||||||||||||||
       101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

       351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
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       117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

       401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
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       134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

       451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
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       151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

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           ||||||||||||||||||||||||||||||||||||||||||||||||||
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 184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

 601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
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 201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

 651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234

 701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
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 751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
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 251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

 801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTCG 850
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 267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

 851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
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 284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300

 901 CCGGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
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 301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317

 951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
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 317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334

1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

1051 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
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1101 CCCGTTGCGCTGGAAGGAGTTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384

1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

1201 TACAGCATGCTGGCGACCTGGAGGAGGCGCACGCCGCGGCGCGAGGCCAC 1250
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417

1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450

1351 CCCAGTCTTCTCAGA 1365
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 451 ProSerLeuLeuArg 455

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seq_documentation_block:
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ID   AAY30934 standard; Protein; 455 AA.
XX
AC   AAY30934;
XX
DT   18-OCT-1999  (first entry)
XX
DE   Human tumour necrosis factor binding protein.
XX
KW   Tumour necrosis factor binding protein; TNF; insoluble protein; agonist;
KW   anti-inflammatory; antimalarial; treatment; septic shock; inflammation;
KW   autoimmune glomerulonephritis; cerebral malaria; immune response;
KW   antagonist; diagnosis.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
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FT                   /label= signal_peptide
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FT   Modified-site   131
FT                   /note= "hypothetical glycosylation site"
FT   Region          212..230
FT                   /note= "transmembrane region"
FT   Modified-site   250
FT                   /note= "hypothetical glycosylation site"
XX
PN   EP939121-A2.
XX
PD   01-SEP-1999.
XX
PF   31-AUG-1990;   90EP-0116707.
XX
PR   20-APR-1990;   90CH-0001347.
PR   12-SEP-1989;   89CH-0003319.
PR   08-MAR-1990;   90CH-0000746.
XX
PA   (HOFF ) HOFFMANN LA ROCHE & CO AG F.
XX
PI   Brockhaus M,  Dembic Z,  Gentz R,  Lesslauer W,  Loetscher H;
PI   Schlaeger E;
XX
DR   WPI; 1999-480840/41.
DR   N-PSDB; AAZ09170.
XX
PT   New insoluble proteins, and fragments, that bind to tumor necrosis
PT   factor, used to treat e.g. septic shock or cerebral malaria
XX
PS   Claim 4a; Fig 1; 25pp; German.
XX
CC   This invention describes novel homogeneous insoluble proteins (I),
CC   their (in)soluble fragments (Ia) and their salts that can bind tumour
CC   necrosis factor (TNF). The products of the invention have
CC   anti-inflammatory and antimalarial activity. (I) and (ia) are used (i)
CC   to treat diseases in which TNF is involved (e.g. septic shock, autoimmune
CC   glomerulonephritis, cerebral malaria, immune responses and inflammation),
CC   (ii) to purify TNF, (iii) to identify TNF (ant)agonists and (iv) for
CC   diagnostic determination of TNF in body fluids. Antibodies raised against
CC   (I) are used for affinity purification of (I). This sequence represents
CC   a tumour necrosis factor binding protein described in the method of
CC   the invention.
XX
SQ   Sequence   455 AA;


alignment_scores:
              Quality: 2487.00             Length:     455
                Ratio:   5.466               Gaps:       0
 Percent Similarity: 100.000   Percent Identity: 100.000
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alignment_block:
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     67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

    251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
        ||||||||||||||||||||||||||||||||||||||||||||||||||
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    301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
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    117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

    401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
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    134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

    451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
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    151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

    501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
        ||||||||||||||||||||||||||||||||||||||||||||||||||
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    601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
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    651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
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    701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
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    751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
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    801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
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    267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

    851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
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    901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
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    951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
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   1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
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   1051 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
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   1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
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   1151 AGATCGATCGCCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
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    384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

   1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
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   1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
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    417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

   1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
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   1351 CCCAGTCTTCTCAGA 1365
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    451 ProSerLeuLeuArg 455

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seq_documentation_block:
ID   AAB36266 standard; Protein; 455 AA.
XX
AC   AAB36266;
XX
DT   20-FEB-2001  (first entry)
XX
DE   Human tumour necrosis factor receptor 1.
XX
KW   Human; death domain containing receptor; DR3-V1; cancer;
KW   autoimmune disorder; inflammation; cardiovascular disorder; infection;
KW   neurodegenerative disease; angiogenesis.
XX
OS   Homo sapiens.
XX
PN   WO200064465-A1.
XX
PD   02-NOV-2000.
XX
PF   21-APR-2000; 2000WO-US10741.
XX
PR   22-APR-1999;   99US-0130488.
PR   28-MAY-1999;   99US-0136741.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
PA   (UNMI ) UNIV MICHIGAN.
PA   (YUGG/) YU G.
```

```
PA   (NIJJ/) NI J.
PA   (GENT/) GENTZ R L.
PA   (DILL/) DILLON P J.
PA   (DIXI/) DIXIT V M
XX
PI   Yu G,  Ni J,  Gentz RL,  Dillon PJ,  Dixit VM;
XX
DR   WPI; 2000 687263/67.
XX
PT   Treating graft versus host disease, cancer, immunodeficiency or an
PT   autoimmune disease comprising administering an antibody to Death Domain
PT   Containing Receptor proteins and a second therapeutic agent -
XX
PS   Disclosure; Fig 3; 273pp; English.
XX
CC   The present invention provides the protein and coding sequences for two
CC   death domain containing receptors, designated DR3 and DR3-V1. These
CC   receptors are involved in apoptosis, and the sequences given can be used
CC   in the treatment of cancers, infections, cardiovascular disorders such as
CC   arrhythmias, ischaemia, aneurysms, arterial occlusive diseases, embolisms
CC   and congenital heart defects, neurodegenerative diseases including
CC   Alzheimer's and Parkinson's diseases, autoimmune disease such as multiple
CC   sclerosis, arthritis, diabetes, Graves' disease, asthma and psoriasis,
CC   and to promote angiogenesis and wound healing.
XX
SQ   Sequence   455 AA;


alignment_scores:
           Quality: 2487.00            Length:     455
             Ratio:   5.466              Gaps:       0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-1 x AAB36266   ..

 Align seg 1/1  to: AAB36266  from: 1  to: 455

       1 ATGGGCCTCTCCACCGTGCCTGACCTGCTGCTGCCACTGGTGCTCCTGGA 50
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       1 MetGlyLeuSerThrValProAspLeuLeuLeuProLeuValLeuLeuGl 17

      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGACTGGTCCCTCACC 100
         |||||||||||||| |||||||||||||||||||||||||||||||||||
      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

     101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGTCCCCAAGGAAAATATATC 150
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150
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     451 AATGGCACGGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
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     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     501 CTGCCATGCAGGCTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
         ||||||||| ||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

     651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
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     217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234

     701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250

     751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
         |||||||||||||||||||||||||||||| |||||||||||||||||||
     251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

     801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

     851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300

     901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317

     951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334

    1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
         |||||||||||||||||||||||||||||||||||||| |||||||||||
     334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

    1051 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367

    1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384

    1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

    1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
         ||||||||||||| ||||||||||||||||||||||||||||||||||||
     401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417

    1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
         |||||||||||| |||||||||||||||||||||||||||||||||||||
     417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

    1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
         |||||||||||| |||||||||||||||||||||||||||||||||||||
     434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450
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   1351 CCCAGTCTTCTCAGA 1365
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    451 ProSerLeuLeuArg 455

seq name: [illegible] AA.[illegible] [A: AAB3[illegible]

seq documentation_block:
ID   AAB37800 standard; Protein; 455 AA.
XX
AC   AAB37800;
XX
DT   23-FEB-2001  (first entry)
XX
DE   Human tumour necrosis factor p55 receptor.
XX
KW   Human; tumour necrosis factor; TNF; TNF-alpha; TNF-beta; p55 receptor;
KW   p75 receptor; antiinflammatory; haemostatic; antibacterial; sepsis;
KW   immunosuppressive; immunomodulator; cardiant; cytostatic; cachexia;
KW   neuroprotective; respiratory; inflammation; infection; Crohn's disease;
KW   multiple sclerosis, autoimmune disorder, cardiovascular disorder;
KW   chronic myelogenous leukaemia, inflammatory bowel disease.
XX
OS   Homo sapiens.
XX
PN   WO200064479-A1.
XX
PD   02-NOV-2000.
XX
PF   26-APR 2000; 2000WO US11700.
XX
PR   27-APR-1999;   99US-0301274.
XX
PA   (ANTI-) ANTIBODY SYSTEMS INC.
XX
PI   Fredeking TM, Ignatyev GM;
XX
DR   WPI; 2000-679646/66.
XX
PT   Novel compositions comprising tetracycline or tetracycline-like
PT   compounds for the treatment and/or prevention of acute inflammatory
PT   responses and diseases, e.g. septic shock and immune complex-induced
PT   colitis -
XX
PS   Disclosure; Page 167-169; 183pp; English.
XX
CC   The present sequence is given in a specification relating to novel
CC   compositions and methods containing tetracycline or tetracycline-like
CC   compounds for treating and/or preventing acute inflammatory responses and
CC   diseases. Such diseases include acute inflammatory conditions associated
CC   with viral haemorrhagic diseases (including diseases caused by
CC   Bunyaviridea, Filoviridae, Flaviviridae or Arenaviridae viruses),
CC   parasitic diseases, bacterial infections, sepsis, cachexia, autoimmune
CC   disorders, acute cardiovascular events, chronic myelogenous leukaemia and
CC   transplanted bone marrow-induced graft-versus-host disease, septic shock,
CC   immune complex-induced colitis, cerebrospinal fluid inflammation,
CC   multiple sclerosis, inflammatory responses associated with trauma,
CC   systemic inflammatory response syndrome (SIRS), adult respiratory
CC   distress syndrome (ARDS), acute liver failure, inflammatory bowel disease
CC   and Crohn's disease
XX
SQ   Sequence   455 AA;


alignment_scores:
             Quality: 2487.00             Length:     455
               Ratio:   5.466               Gaps:       0
  Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
  US-09-525-998A-1 x AAB37800   ..

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       ||||||||||||||||||||||||||||||||||||||||||||||||||
    17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

   101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGTCCCCAAGGAAAATATATC 150
       ||||||||||||||||||||||||||||||||||||||||||||||||||
    34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

   151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
       ||||||||||||||||||||||||||||||||||||||||||||||||||
    51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

   201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
       ||||||||||||||||||||||||||||||||||||||||||||||||||
    67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

   251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
       ||||||||||||||||||||||||||||||||||||||||||||||||||
    84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

   301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
       ||||||||||||||||||||||||||||||||||||||||||||||||||
   101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

   351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
       ||||||||||||||||||||||||||||||||||||||||||||||||||
   117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

   401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
       ||||||||||||||||||||||||||||||||||||||||||||||||||
   134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

   451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
       ||||||||||||||||||||||||||||||||||||||||||||||||||
   151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

   501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
       ||||||||||||||||||||||||||||||||||||||||||||||||||
   167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

   551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
       ||||||||||||||||||||||||||||||||||||||||||||||||||
   184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

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   201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

   651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
       ||||||||||||||||||||||||||||||||||||||||||||||||||
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       ||||||||||||||||||||||||||||||||||||||||||||||||||
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       ||||||||||||||||||||||||||||||||||||||||||||||||||
   251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

   801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
       ||||||||||||||||||||||||||||||||||||||||||||||||||
   267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

   851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
       ||||||||||||||||||||||||||||||||||||||||||||||||||
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   901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
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     951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
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     317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334

    1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

    1051 CTAGACACTGATGACCCGGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367

    1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384

    1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

    1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417

    1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

    1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450

    1351 CCCAGTCTTCTCAGA 1365
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     451 ProSerLeuLeuArg 455

seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA2000.DAT:AAB26984

seq_documentation_block:
ID   AAB26984 standard; Protein; 455 AA.
XX
AC   AAB26984;
XX
DT   02-FEB-2001  (first entry)
XX
DE   Human TNFR 1.
XX
KW   Human; TNFR 1; tumour necrosis factor; TR9 receptor; immunosuppressive;
KW   antiinflammatory, cardiant, antiasthmatic, antidiabetic, antiallergic;
KW   antiathritic; antirheumatic; anti-HIV; anticonvulsant; cytostatic;
KW   neuroprotective, gene therapy, Death Domain Containing Receptor 6;
KW   common variable immunodeficiency, X-linked agammaglobulinaemia,
KW   severe combined immunodeficiency, Wiskott-Aldrich syndrome,
KW   autoimmune disease, rheumatoid arthritis, allergic encephalomyelitis;
KW   multiple sclerosis, diabetes mellitus, asthma, epilepsy, cancer,
KW   cardiovascular disease, neurological disease, protein coordinate data.
XX
OS   Homo sapiens.
XX
PN   WO200056862-A1.
XX
PD   28-SEP-2000.
XX
PF   16-MAR-2000; 2000WO-US06831.
XX
PR   24-MAR-1999;   99US-0126019.
PR   14-MAY-1999;   99US-0134220.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
XX
PI   Ni J,  Gentz RL,  Yu G,  Fan P;
XX
DR   WPI; 2000-594575/56.
XX
PT   Nucleic acid molecule encoding a human tumor necrosis factor receptor,
PT   known as TR9, useful for treating, preventing and diagnosing severe
PT   combined immunodeficiency, autoimmune diseases, HIV infection, epilepsy
PT   and cancer -
XX
PS   Disclosure; Fig 2; 220pp; English.
XX
CC   The present sequence is TNFR 1, a member of the tumour necrosis factor
CC   receptor family. A novel human tumour necrosis factor receptor,
CC   designated TR9, has been isolated. The TR9 receptor is also known as
CC   Death Domain Containing Receptor 6. TR9 polypeptides, polynucleotides or
CC   agonists are useful for treating, preventing or diagnosing common
CC   variable immunodeficiency, X-linked agammaglobulinaemia, severe combined
CC   immunodeficiency, and Wiskott Aldrich syndrome, autoimmune diseases (such
CC   as rheumatoid arthritis, allergic encephalomyelitis, multiple sclerosis,
CC   diabetes mellitus and asthma), HIV infection, epilepsy, cancer,
CC   cardiovascular diseases and other neurological diseases.
XX
SQ   Sequence   455 AA;

alignment_scores:
           Quality: 2487.00             Length:     455
             Ratio:   5.466               Gaps:       0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-1 x AAB26984   ..

 Align seg 1/1  to: AAB26984  from: 1  to: 455

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     101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGTCCCCAAGGAAAATATATC 150
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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     201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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 151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

 501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

 551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

 601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
     ||||||||||||||||||||||||||||||||||||||||||||||||||
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 217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234

 701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
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 234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250

 751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
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 251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

 801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

 851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300

 901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317

 951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334

1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

1051 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367

1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384

1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417

1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCC 1350
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450

1351 CCCAGTCTTCTCAGA 1365
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 451 ProSerLeuLeuArg 455
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seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA2000.DAT:AAB23446

seq_documentation_block:
ID   AAB23446 standard; Protein; 455 AA.
XX
AC   AAB23446;
XX
DT   12 JAN 2001  (first entry)
XX
DE   Human tumour necrosis factor receptor 1 protein.
XX
KW   TNFR1; tumour necrosis factor receptor; polymorphism; human;
KW   tumour; cancer; apoptosis; bacterial infection.
XX
OS   Homo sapiens.
XX
PN   WO200050436-A1.
XX
PD   31-AUG-2000.
XX
PF   23-FEB-2000; 2000WO-US04606.
XX
PR   23-FEB-1999;   99US-0121314.
XX
PA   (GENA-) GENAISSANCE PHARM INC.
PA   (NAND/) NANDABALAN K.
PA   (SCHU/) SCHULZ V P.
PA   (STEP/) STEPHENS J C.
PA   (CHEW/) CHEW A.
XX
PI   Nandabalan K,  Schulz VP,  Stephens JC,  Chew A;
XX
DR   WPI; 2000-543909/49.
DR   N-PSDB; AAA95105.
XX
PT   Polynucleotides comprising polymorphic variants of a reference sequence
PT   for tumour necrosis factor receptor 1 (TNFR1), useful for studying the
PT   biological function of TNFR1 and identifying drugs targeting the
PT   protein for treating disorders -
XX
PS   Claim 10; Fig 5; 79pp; English.
XX
CC   The present invention relates to polymorphic variants of the tumour
CC   necrosis factor receptor 1 (TNFR1) gene. The present sequence is
CC   the TNFR1 protein. The sequence of the whole gene is given in AAA95102,
CC   AAA95103 and AAA95104. The polymorphisms were identified by amplifying
CC   and sequencing regions of the gene. Twelve polymorphic loci
CC   were discovered. Of these twelve polymorphisms, four can cause a
CC   change in the TNFR1 protein.  The TNFR1 polymorphisms may be useful
CC   for studying the biological function of TNFR1 as well as for
CC   identifying drugs targeting the protein for treatment of disorders
CC   related to its abnormal expression or function such as tumours,
CC   apoptosis related disorders and bacterial infection.
XX
SQ   Sequence   455 AA;


alignment_scores:
           Quality: 2487.00            Length:    455
             Ratio:  5.466               Gaps:      0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-1 x AAB23446   ..

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       1 MetGlyLeuSerThrValProAspLeuLeuLeuProLeuValLeuLeuGl 17

      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGACTGGTCCCTCACC 100
```

```
         ||||||||||||||||||||||||||||||||||||||||||||||||||
  17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

 101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGTCCCCAAGGAAAATATATC 150
     ||||||||||||||||||||||||||||||||||||||||||||||||||
  34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

 151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
     ||||||||||||||||||||||||||||||||||||||||||||||||||
  51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

 201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
     ||||||||||||||||||||||||||||||||||||||||||||||||||
  67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

 251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
     ||||||||||||||||||||||||||||||||||||||||||||||||||
  84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

 301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

 351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

 401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
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 134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

 451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
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 151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

 501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

 551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
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 601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
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 201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

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 701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTCTGCGGCAAA 750
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 801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
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 267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

 851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
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 901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
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 301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317

 951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTGGCCTCCGACCCCA 1000
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1051 CTAGACACTGATGACCCGGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
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 351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367

1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
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1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
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 384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
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1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
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 417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

1301 TGGAGGACATCCAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
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1351 CCCAGTCTTCTCAGA 1365
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 451 ProSerLeuLeuArg 455

seq_name: /SIDS2/gcgdata/geneseq/geneseqp/AA2000.DAT:AAB01336

seq_documentation_block:
ID   AAB01336 standard; Protein; 455 AA.
XX
AC   AAB01336;
XX
DT   25-SEP-2000  (first entry)
XX
DE   TNF-R1 death receptor.
XX
KW   UL144, death receptor, apoptosis, programmed cell death; FAS;
KW   TNF-R1; TRAMP; DR-6; TRAIL; modulation; treatment; cancer; virus;
KW   human.
XX
OS   Homo sapiens.
XX
PN   WO200034335-A2.
XX
PD   15-JUN-2000.
XX
PF   03-DEC-1999;   99WO-US26035.
XX
PR   04-DEC-1998;   98US-0205018.
XX
PA   (SCHE ) SCHERING CORP.
XX
PI   Leong C,  Phillips JH;
XX
DR   WPI; 2000-423383/36.
XX
PT   Purified or recombinant polypeptide for modulating apoptosis comprises
PT   a sequence which binds to an antibody specific for UL144 or its
PT   fragments
XX
PS   Disclosure; Page 65-67; 76pp; English.
XX
CC   A pure or recombinant polypeptide which binds to a polyclonal antibody
CC   specific for the mature UL144 is useful for screening molecules which
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CC   block induction of apoptosis or interfere with antiapoptotic activity.
CC   The polypeptide is also useful for modulating apoptosis and useful in
CC   treatment of conditions associated with abnormal physiology or
CC   development, such as cancer or degenerative conditions and for
CC   regulation of viral infection and replication. At least five
CC   different death receptors are known, which include the CD95
CC   (Fas/APO-1), the TNF receptor-1, TNF receptor apoptosis-mediated
CC   protein (TRAMP), death receptor-6 (DR-6), and TNF-related
CC   apoptosis-inducing ligand (TRAIL) receptors 1, 2 and 4
XX
SQ   Sequence   455 AA;


alignment_scores:
          Quality: 2487.00              Length:     455
            Ratio:   5.466                Gaps:       0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-1 x AAB01336    ..

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      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGACTGGTCCCTCACC 100
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

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      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
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      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     301 AGCTGCTCCAAATGCCGAAAGGAAATGGCTCAGGTGGAGATCTCTTCTTG 350
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
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     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

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     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

     651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234

     701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250

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         ||||||||||||||||||||||||||||||||||||||||||||||||||
     251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

     801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

     851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
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     284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300

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     301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317

     951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
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     317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334

    1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
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    1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
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    1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
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    1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
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    1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

    1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
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    1351 CCCAGTCTTCTCAGA 1365
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     451 ProSerLeuLeuArg 455

seq_name: /SIDS2/qcgdata/geneseq/geneseqp/AA2001.DAT:AAB36697

seq_documentation_block:
ID   AAB36697 standard; Protein; 455 AA.
XX
AC   AAB36697;
XX
DT   15-MAR-2001  (first entry)
XX
DE   Human tumour necrosis factor receptor TNFR1 protein SEQ ID NO:3.
XX
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KW   Human; tumour necrosis factor receptor 5; TRID; TNFR-5; TR5; nootropic;
KW   TRAIL receptor without intracellular domain; diagnosis; cytostatic;
KW   tumour necrosis factor related apoptosis inducing ligand; vasotropic;
KW   immunosuppressive; neuroprotective; antiviral; antiinflammatory;
KW   anticonvulsant; antiparasitic; cardiant; anti-HIV; antiparkinsonian;
KW   gene therapy; restenosis; graft versus host disease; tumour; cancer;
KW   apoptotic cell death related disease; autoimmune disorder;
KW   cardiovascular disorder; viral infection.
XX
OS   Homo sapiens.
XX
PN   WO200071150-A1.
XX
PD   30-NOV-2000.
XX
PF   18-MAY-2000; 2000WO-US13515.
XX
PR   20-MAY-1999;   99US-0135164.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
XX
PI   Wei Y,  Ruben SM,  Gentz RL,  Ni J;
XX
DR   WPI; 2001-041051/05.
XX
PT   Nucleic acid encoding a TRID polypeptide, also referred to as tumor
PT   necrosis factor receptor 5, useful in the diagnosis, treatment or
PT   prevention of cancer, autoimmune disorders and viral infection -
XX
PS   Disclosure; Fig 2; 285pp; English.
XX
CC   The present invention describes the human TRID protein (tumour necrosis
CC   factor (TNF) related apoptosis inducing ligand (TRAIL) receptor without
CC   intracellular domain, also referred to as tumour necrosis factor
CC   receptor 5 (TNFR-5 or TR5)). TRID has cytostatic, immunosuppressive,
CC   nootropic, neuroprotective, antiviral, antiinflammatory, anticonvulsant,
CC   antiparasitic, cardiant, anti HIV, antiparkinsonian and vasotropic
CC   activities, and can be used in gene therapy. The TRID polynucleotides
CC   are useful for detecting complementary polynucleotides. TRID proteins and
CC   polynucleotides are useful in the treatment of tumours, resistance to
CC   parasite, bacteria and viruses, restenosis and graft versus host disease.
CC   They are also useful for inducing proliferation of T-cells, endothelial
CC   cells and certain haematopoietic cells, to regulate antiviral responses
CC   and to prevent certain autoimmune diseases after stimulation of TRID by
CC   an agonist or TRAIL binding facilitator. The antibodies which bind TRID
CC   polypeptides are useful for treating and/or preventing diseases
CC   associated with increased or decreased apoptotic cell death. The TRID
CC   polynucleotides, proteins, antibodies, agonists and antagonists are
CC   useful in the diagnosis, treatment or prevention of: (a) cancer;
CC   (b) autoimmune disorders; (c) diseases associated with increased
CC   apoptosis; (d) cardiovascular disorders; and (e) viral infection. The
CC   present sequence represents a tumour necrosis factor receptor used in
CC   comparison with TRID in the exemplification of the present invention.
XX
SQ   Sequence   455 AA;


alignment_scores:
           Quality: 2487.00              Length:     455
             Ratio:  5.466                 Gaps:       0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
 US-09-525-998A-1 x AAB36697   ..

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      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGACTGGTCCCTCACC 100
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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     101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGTCCCCAAGGAAAATATATC 150
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     151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
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      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
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     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
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     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
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     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
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     184 snCysLysLysSerLeuGluCysThrLysLeuCysLeuProGlnIleGlu 200

     601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

     651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
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     217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234

     701 ATCGCTACCAACGCTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250

     751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

     801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

     851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300

     901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317

     951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
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     317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334
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    1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
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     334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

    1051 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367

    1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisC 384

    1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

    1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGCCGCGAGGCCAC 1250
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417

    1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

    1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450

    1351 CCCAGTCTTCTCAGA 1365
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     451 ProSerLeuLeuArg 455

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seq_documentation_block:
ID   AAB37677 standard, protein; 455 AA.
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AC   AAB37677;
XX
DT   02-MAR-2001  (first entry)
XX
DE   Human 30 kDa TNF inhibitor precursor.
XX
KW   TNF inhibitor; antiinflammatory; Tumour Necrosis Factor; interleukin
KW   IL-1; inflammatory disease; degenerative disease; human.
XX
OS   Homo sapiens.
XX
PN   US6143866-A.
XX
PD   07-NOV-2000.
XX
PF   19-JAN-1995;   95US-0375242.
XX
PR   19-JUL-1990;   90US-0555274.
PR   09-JUL-1993;   93US-0090366.
PR   18-JUL-1989;   89US-0381080.
PR   11-DEC-1989;   89US-0450329.
PR   07-FEB-1990;   90US-0479661.
XX
PA   (AMGE-) AMGEN INC.
XX
PI   Squires C,  King MW,  Hale KK,  Brewer MT,  Thompson RC;
PI   Vanderslice RW,  Vannice J,  Kohno T;
XX
DR   WPI; 2001-006443/01
DR   N-PSDB; AAC83946.
XX
PT   Novel 30 kDa tumor necrosis factor inhibitor analog comprising a
PT   non-native cysteine residue cross linked with polyethylene glycol,
PT   useful for treating inflammatory and degenerative diseases mediated by
PT   TNF -
XX
PS   Example 6, Fig 21, 82pp, English.
XX
CC   The present invention relates to Tumour Necrosis Factor (TNF) inhibitors
CC   (see AAB37676 and AAB37685), which have TNF inhibitory activity. The
CC   novel TNF inhibitors of the present invention are useful as therapeutic
CC   agents for inhibiting the activity of TNF and interleukin (IL-1), and
CC   for treating inflammatory and degenerative diseases mediated by TNF. The
CC   present sequence is the precursor for 30 kDa TNF inhibitor. The 30 kDa
CC   TNF inhibitor can inhibit TNF alpha.
XX
SQ   Sequence   455 AA;


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            Quality:  2487.00             Length:     455
              Ratio:   5.466                Gaps:       0
 Percent Similarity: 100.000   Percent Identity: 100.000

alignment_block:
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      51 GCTGTTGGTGGGAATATACCCCTCAGGGGTTATTGGACTGGTCCCTCACC 100
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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     101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGTCCCCAAGGAAAATATATC 150
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      34 euGlyAspArgGluLysArgAspSerValCysProGlnGlyLysTyrIle 50

     151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

     301 AGCTGCTCCAAATGCCGAAAGGAAATGGGTCAGGTGGAGATCTCTTCTTG 350
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

     351 CACAGTGGACCGGGACACCGTGTGTGGCTGCAGGAAGAACCAGTACCGGC 400
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

     451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

     501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
         ||||||||||||||||||||||||||||||||||||||||||||||||||
     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

     551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
         ||||||||||||||||||||||||||||||||||||||||||||||||||
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     601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
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        ||||||||||||||||||||||||||||||||||||||||||||||||||
    217 lIlePhePheGlyLeuCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234

    701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
        ||||||||||||||||||||||||||||||||||||||||||||||||||
    234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250

    751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
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    251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

    801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
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    267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

    851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
        ||||||||||||||||||||||||||||||||||||||||||||||||||
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    901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
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    951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
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   1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
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    334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

   1051 CTAGACACTGATGACCCCGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
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    351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367

   1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
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   1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
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    417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

   1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
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    434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450

   1351 CCCAGTCTTCTCAGA 1365
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seq_documentation_block:
ID   AAR11082 standard; Protein; 455 AA.
XX
AC   AAR11082;
XX
DT   24-MAY-1991  (first entry)
XX
DE   Human 55kD TNF-binding protein.
```

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XX
KW   Tumour Necrosis Factor, binding proteins, septic shock;
KW   autoimmune glomerulonephritis; lymphokine; cytokine.
XX
FH   Key                 Location/Qualifiers
FT   Modified site       54
FT                       /label= putative N-glycosylation site
FT   Modified-site       145
FT                       /label- putative N-glycosylation site
FT   Modified-site       151
FT                       /label- putative N glycosylation site
FT   Modified-site       270
FT                       /label  putative N glycosylation site
FT   Region              212..230
FT                       /label- transmembrane region
FT   Peptide             1..28
FT                       /label- signal peptide
XX
PN   EP417563-A.
XX
PD   20-MAR-1991.
XX
PF   31-AUG-1990;   90EP-0116707.
XX
PR   20-APR-1990;   90CH-0001347.
PR   12-SEP-1989;   89CH-0003319.
PR   08-MAR-1990;   90CH-0000746.
XX
PA   (HOFF ) HOFFMANN-LA ROCHE AG.
XX
PI   Brockhaus M,  Dembic Z,  Gentz R,  Lesslauer W,  Lotscher H;
PI   Schlaeger EJ;
XX
DR   WPI; 1991-081851/12.
DR   N-PSDB; AAQ10955.
XX
PT   Insoluble tumour necrosis factor binding proteins - and DNA
PT   encoding them, useful in pharmaceutical prods. and for antibody
PT   prodn.
XX
PS   Claim 1; Fig 1; 26pp; German.
XX
CC   Partial amino acid sequences were determined for the 55 and 75kD
CC   TNF BPs (see AAR11072-R11081) and oligonucleotide primers were
CC   synthesised based on these partial sequences. The primers were used
CC   to produce a cDNA fragment for use as a probe to screen a human
CC   placental cDNA bank constructed in lambda gt11. Positive clones were
CC   identifed and sequenced. DNA constructs comprising the TNF BP coding
CC   sequence may also contain a fragment encoding a human Ig domain.
CC   Recombinant constructs are used to transform cells to confer
CC   improved TNF-binding properties.
CC   See also AAQ10956.
XX
SQ   Sequence   455 AA;


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             Quality: 2484.00               Length:     455
               Ratio:  5.459                  Gaps:       0
 Percent Similarity: 100.000   Percent Identity: 99.780

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 151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
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  51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

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     ||||||||||||||||||||||||||||||||||||||||||||||||||
  67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

 251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
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 101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

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 134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

 451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 151 AsnGlyThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

 501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

 551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
     ||||||||||||||||||||||||||||||||||||||||||||||||||
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 651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
     |||||||||||||:::||||||||||||||||||||||||||||||||||
 217 lIlePhePheGlyValCysLeuLeuSerLeuLeuPheIleGlyLeuMetT 234

 701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGAAAA 750
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 751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
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 267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

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1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
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1051 CTAGACACTGATGACCCGGCGACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
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1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
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1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
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 401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417

1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
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1351 CCCAGTCTTCTCAGA 1365
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 451 ProSerLeuLeuArg 455

seq_name  /SIDS2/gcgdata/geneseq/geneseqp/AA1992.DAT:AAR20787

seq_documentation_block:
ID   AAR20787 standard, Protein; 455 AA.
XX
AC   AAR20787;
XX
DT   11-MAY-1992  (first entry)
XX
DE   TNF-alpha binding protein.
XX
KW   Tumour necrosis factor alpha; autoimmune diseases; cachectin;
KW   extracellular domain.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Peptide         1..40
FT                   /note- "signal peptide"
FT   Peptide         41..455
FT                   /note- "mature peptide"
FT   Domain          30..199
FT                   /note- "extracellular domain"
FT   Domain          212..234
FT                   /note- "transmembrane domain"
FT   Modified-site   145..147
FT                   /note- "potential N-glycosylation site"
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FT                   /note- "potential N-glycosylation site"
XX
PN   GB2246569-A.
XX
PD   05-FEB-1992.
XX
PF   15-JUN-1990;   90GB-0013410.
XX
PR   15-JUN-1990;   90GB-0013410.
XX
PA   (CHAR-) CHARING CROSS SUNLE.
XX
PI   Feldman M,  Gray P,  Turner M,  Brennan F;
```

```
XX
DR   WPI; 1992-043613/06.
DR   N-PSDB; AAQ20973.
XX
PT   New tumour necrosis factor alpha binding protein and polypeptide
PT   - useful in treating cachexia, sepsis and auto immune diseases
PT   e.g. rheumatoid arthritis
XX
PS   Disclosure; Fig 1; 25pp; English.
XX
CC   The amino acid sequence is that of tumour necrosis factor alpha
CC   binding protein which contains the extracellular domain of human TNF
CC   alpha receptor. It is soluble and can be used in the regulation of
CC   TNF-mediated responses by binding and sequestering the cytokine. It
CC   can therefore be used therapeutically to treat disorders such as
CC   cachexia, sepsis and autoimmune diseases, specifically rheumatoid
CC   arthritis.
XX
SQ   Sequence   455 AA;


alignment_scores:
           Quality: 2481.00              Length.     455
             Ratio:  5.453                Gaps:        0
 Percent Similarity: 100.000   Percent Identity: 99.560

alignment_block.
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 Align seq 1/1  to: AAR20787  from: 1  to: 455

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      17 uLeuLeuValGlyIleTyrProSerGlyValIleGlyLeuValProHisL 34

     101 TAGGGGACAGGGAGAAGAGAGATAGTGTGTGTCCCCAAGGAAAATATATC 150
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      34 euGlyAspArgGluArgLysAspSerValCysProGlnGlyLysTyrIle 50

     151 CACCCTCAAAATAATTCGATTTGCTGTACCAAGTGCCACAAAGGAACCTA 200
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      51 HisProGlnAsnAsnSerIleCysCysThrLysCysHisLysGlyThrTy 67

     201 CTTGTACAATGACTGTCCAGGCCCGGGGCAGGATACGGACTGCAGGGAGT 250
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      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
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      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

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     101 SerCysSerLysCysArgLysGluMetGlyGlnValGluIleSerSerCy 117

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     117 sThrValAspArgAspThrValCysGlyCysArgLysAsnGlnTyrArgH 134

     401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
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     134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

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     201 AsnValLysGly hrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

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     701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
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     251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProGl 267

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     317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334

    1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
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     334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

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seq_name: [illegible] AAR12197

seq_documentation_block:
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ID   AAR42197 standard; Protein; 455 AA.
XX
AC   AAR42197;
XX
DT   13-MAY-1994  (first entry)
XX
DE   p55 Tumour necrosis factor receptor.
XX
KW   TNF; tumour necrosis factor; receptor; disease; autoimmunity;
KW   rheumatoid arthritis; graft rejection; graft vs. host; septic shock;
KW   effector protein.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Region          1..21
FT                   /label= Leader peptide.
FT   Domain          183..205
FT                   /label= Transmembrane domain.
XX
PN   EP568925-A.
XX
PD   10-NOV-1993.
XX
PF   29-APR-1993;   93EP-0106981.
XX
PR   03-MAY-1992;   92IL-0101769.
XX
PA   (YEDA ) YEDA RES & DEV CO LTD.
XX
PI   Brakebusch C,  Wallach D;
XX
DR   WPI; 1993-353057/45.
DR   N-PSDB; AAQ50870.
XX
PT   Modulating activity of tumour necrosis factor receptor - using
PT   peptide(s), antibodies, etc. which interact with critical regions
PT   of receptor or effector protein, for controlling auto-immune
PT   disease, septic shock, etc.
XX
PS   Claim 2; Figure 1; 17pp; English.
XX
CC   Modification of the tumour necrosis factor receptor by mutation or
CC   deletion modulates signal transduction and/or cleavage effected by
CC   the receptor.  This modulation of activity can also be achieved
CC   using effector proteins which interact with the TNF receptor
CC   Molecules which interact with the TNF receptor or the effector
CC   proteins can be used to treat or prevent diseases associated with
CC   TNF activity e.g. autoimmune disease; rheumatoid arthritis; graft
CC   rejection; graft vs  host disease or septic shock.  They can also
CC   be used to treat overdoses of exogenous TNF.  Specific deletions
CC   include amino acid residues 405-426 from which it was discovered
CC   that amino acids 405-414, or part of them, are essential for the
CC   signalling of the human p55 TNF-R for the cytotoxic effect of TNF
CC   whereas amino acids 415-426 are not essential.  Also residues
CC   170-174, 174-179 or both i.e 170-179 were deleted.  This region of
CC   amino acids, or part of, when deleted, abolished shedding of the
CC   soluble extracellular forms of the protein.
XX
SQ   Sequence   455 AA;


alignment_scores:
           Quality: 2478.00              Length:     455
             Ratio:    5.446               Gaps:       0
 Percent Similarity: 100.000   Percent Identity:  99.560

alignment_block:
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     167 rCysHisAlaGlyPhePheLeuArgGluAsnGluCysValSerCysSerA 184

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1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
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 334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

1051 CTAGACACTGATGACCCCGCCACGCTGTACGCCGTGGTGGAGAACGTGCC 1100
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1351 CCCAGTCTTCTCAGA 1365
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 451 ProSerLeuLeuArg 455

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seq_documentation_block:
ID   AAR51034 standard; Protein; 455 AA.
XX
AC   AAR51034;
XX
DT   13-MAY-1994  (first entry)
XX
DE   Mutant p55 tumour necrosis factor receptor.
XX
KW   TNF; tumour necrosis factor; receptor; disease; autoimmunity;
KW   rheumatoid arthritis; graft rejection; graft vs. host; septic shock,
KW   effector protein.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Region          1..21
FT                   /label- Leader peptide.
FT   Domain          183..205
FT                   /label- Transmembrane domain.
XX
PN   EP568925-A.
XX
PD   10-NOV-1993.
XX
PF   29-APR-1993;   93EP-0106981.
XX
PR   03-MAY-1992;   92IL-0101769.
XX
PA   (YEDA ) YEDA RES & DEV CO LTD.
XX
PI   Brakebusch C,  Wallach D;
XX
```

```
DR   WPI; 1993 [illegible]/45.
DR   N-PSDB; AAQ50870.
XX
PT   Modulating activity of tumour necrosis factor receptor   using
PT   peptide(s), antibodies, etc. which interact with critical regions
PT   of receptor or effector protein, for controlling auto immune
PT   disease, septic shock, etc.
XX
PS   Claim 5; Figure 1; 17pp; English.
XX
CC   Modification of the tumour necrosis factor receptor by mutation or
CC   deletion modulates signal transduction and/or cleavage effected by
CC   the receptor.  This modulation of activity can also be achieved
CC   using effector proteins which interact with the TNF receptor.
CC   Molecules which interact with the TNF receptor or the effector
CC   proteins can be used to treat or prevent diseases associated with
CC   TNF activity e.g. autoimmune disease; rheumatoid arthritis; graft
CC   rejection; graft vs. host disease or septic shock.  They can also
CC   be used to treat overdoses of exogenous TNF.  Specific deletions
CC   include amino acid residues 405-426 from which it was discovered
CC   that amino acids 405 414, or part of them, are essential for the
CC   signalling of the human p55 TNF-R for the cytotoxic effect of TNF
CC   whereas amino acids 415 426 are not essential.  Also residues
CC   170-174, 174-179 or both i.e 170-179 were deleted.  This region of
CC   amino acids, or part of, when deleted, abolished shedding of the
CC   soluble extracellular forms of the protein.  This sequence
CC   corresponds to the wild type protein disclosed in AAR42197 except
CC   that alanine at postion 197 has been substituted in place of serine.
CC   The substitution inhibits cleavage of the soluble form of the
CC   protein.
XX
SQ   Sequence   455 AA;


alignment_scores:
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             Ratio:  5.440                 Gaps:      0
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      67 rLeuTyrAsnAspCysProGlyProGlyGlnAspThrAspCysArgGluC 84

     251 GTGAGAGCGGCTCCTTCACCGCTTCAGAAAACCACCTCAGACACTGCCTC 300
         ||||||||||||||||||||||||||||||||||||||||||||||||||
      84 ysGluSerGlySerPheThrAlaSerGluAsnHisLeuArgHisCysLeu 100

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 401 ATTATTGGAGTGAAAACCTTTTCCAGTGCTTCAATTGCAGCCTCTGCCTC 450
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 134 isTyrTrpSerGluAsnLeuPheGlnCysPheAsnCysSerLeuCysLeu 150

 451 AATGGGACCGTGCACCTCTCCTGCCAGGAGAAACAGAACACCGTGTGCAC 500
     |||:::||||||||||||||||||||||||||||||||||||||||||||
 151 AsnAlaThrValHisLeuSerCysGlnGluLysGlnAsnThrValCysTh 167

 501 CTGCCATGCAGGTTTCTTTCTAAGAGAAAACGAGTGTGTCTCCTGTAGTA 550
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 551 ACTGTAAGAAAAGCCTGGAGTGCACGAAGTTGTGCCTACCCCAGATTGAG 600
     |||||||||||||||||:::||||||||||||||||||||||||||||||
 184 snCysLysLysSerLeuGlnCysThrLysLeuCysLeuProGlnIleGlu 200

 601 AATGTTAAGGGCACTGAGGACTCAGGCACCACAGTGCTGTTGCCCCTGGT 650
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 201 AsnValLysGlyThrGluAspSerGlyThrThrValLeuLeuProLeuVa 217

 651 CATTTTCTTTGGTCTTTGCCTTTTATCCCTCCTCTTCATTGGTTTAATGT 700
     |||||||||||||||||||||||||:::||||||||||||||||||||||
 217 lIlePhePheGlyLeuCysLeuLeuAlaLeuLeuPheIleGlyLeuMetT 234

 701 ATCGCTACCAACGGTGGAAGTCCAAGCTCTACTCCATTGTTTGTGGGAAA 750
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 234 yrArgTyrGlnArgTrpLysSerLysLeuTyrSerIleValCysGlyLys 250

 751 TCGACACCTGAAAAAGAGGGGGAGCTTGAAGGAACTACTACTAAGCCCCT 800
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 251 SerThrProGluLysGluGlyGluLeuGluGlyThrThrThrLysProLe 267

 801 GGCCCCAAACCCAAGCTTCAGTCCCACTCCAGGCTTCACCCCCACCCTGG 850
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 267 uAlaProAsnProSerPheSerProThrProGlyPheThrProThrLeuG 284

 851 GCTTCAGTCCCGTGCCCAGTTCCACCTTCACCTCCAGCTCCACCTATACC 900
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 284 lyPheSerProValProSerSerThrPheThrSerSerSerThrTyrThr 300

 901 CCCGGTGACTGTCCCAACTTTGCGGCTCCCCGCAGAGAGGTGGCACCACC 950
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 301 ProGlyAspCysProAsnPheAlaAlaProArgArgGluValAlaProPr 317

 951 CTATCAGGGGGCTGACCCCATCCTTGCGACAGCCCTCGCCTCCGACCCCA 1000
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 317 oTyrGlnGlyAlaAspProIleLeuAlaThrAlaLeuAlaSerAspProI 334

1001 TCCCCAACCCCCTTCAGAAGTGGGAGGACAGCGCCCACAAGCCACAGAGC 1050
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 334 leProAsnProLeuGlnLysTrpGluAspSerAlaHisLysProGlnSer 350

1051 CTAGACACTGATGACCCCGCGACCCTGTACGCCGTGGTGGAGAACGTGCC 1100
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 351 LeuAspThrAspAspProAlaThrLeuTyrAlaValValGluAsnValPr 367

1101 CCCGTTGCGCTGGAAGGAATTCGTGCGGCGCCTAGGGCTGAGCGACCACG 1150
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 367 oProLeuArgTrpLysGluPheValArgArgLeuGlyLeuSerAspHisG 384

1151 AGATCGATCGGCTGGAGCTGCAGAACGGGCGCTGCCTGCGCGAGGCGCAA 1200
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 384 luIleAspArgLeuGluLeuGlnAsnGlyArgCysLeuArgGluAlaGln 400

1201 TACAGCATGCTGGCGACCTGGAGGCGGCGCACGCCGCGGCGCGAGGCCAC 1250
     ||||||||||||||||||||||||||||||||||||||||||||||||||
 401 TyrSerMetLeuAlaThrTrpArgArgArgThrProArgArgGluAlaTh 417

1251 GCTGGAGCTGCTGGGACGCGTGCTCCGCGACATGGACCTGCTGGGCTGCC 1300
     ||||||||||||||||||||||||||||||||||||||||||||||||||
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 417 rLeuGluLeuLeuGlyArgValLeuArgAspMetAspLeuLeuGlyCysL 434

1301 TGGAGGACATCGAGGAGGCGCTTTGCGGCCCCGCCGCCCTCCCGCCCGCG 1350
     |||||||||||||||||||||||||||||||||.||||||||||||||||
 434 euGluAspIleGluGluAlaLeuCysGlyProAlaAlaLeuProProAla 450

1351 CCCAGTCTTCTCAGA 1365
     |||||||||||||||
 451 ProSerLeuLeuArg 455
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